

SEQUENCE LISTING

<110> KISHIMOTO, Tadamitsu
NAGASAWA, Takashi
TACHIBANA, Kazunobu
CHUGAI SEIYAKU KABUSIKI KAISHA

<120> Vascularization Inhibitors

<130> 46124-5042-US

<140> US 09/646,785

<141> 2001-02-16

<150> PCT/JP99/01448

<151> 1999-03-23

<150> JP10/95448

<151> 1998-03-24

<160> 12

<210> 1

<211> 352

<212> PRT

<213> Mus

<400> 1

Met	Glu	Gly	Ile	Ser	Ile	Tyr	Thr	Ser	Asp	Asn	Tyr	Thr	Glu	Glu		
				5					10					15		
Met	Gly	Ser	Gly	Asp	Tyr	Asp	Ser	Met	Lys	Glu	Pro	Cys	Phe	Arg		
				20					25					30		
Glu	Glu	Asn	Ala	Asn	Phe	Asn	Lys	Ile	Phe	Leu	Pro	Thr	Ile	Tyr		
				35					40					45		
Ser	Ile	Ile	Phe		Thr	Gly	Ile	Val	Gly	Asn	Gly	Leu	Val	Ile		
				50					55					60		
Leu	Val	Met	Gly	Tyr	Gln	Lys	Lys	Leu	Arg	Ser	Met	Thr	Asp	Lys		
				65					70					75		
Tyr	Arg	Leu	His	Leu	Ser	Val	Ala	Asp	Leu	Leu	Phe	Val	Ile	Thr		
				80					85					90		
Leu	Pro	Phe	Trp	Ala	Val	Asp	Ala	Val	Ala	Asn	Trp	Tyr	Phe	Gly		
				95					100					105		
Asn	Phe	Leu	Cys	Lys	Ala	Val	His	Val	Ile	Tyr	Thr	Val	Asn	Leu		
				110					115					120		
Tyr	Ser	Ser	Val	Leu	Ile	Leu	Ala	Phe	Ile	Ser	Leu	Asp	Arg	Tyr		
				125					130					135		
Leu	Ala	Ile	Val	His	Ala	Thr	Asn	Ser	Gln	Arg	Pro	Arg	Lys	Leu		
				140					145					150		
Leu	Ala	Glu	Lys	Val	Val	Tyr	Val	Gly	Val	Trp	Ile	Pro	Ala	Leu		
				155					160					165		
Leu	Leu	Thr	Ile	Pro	Asp	Phe	Ile	Phe	Ala	Asn	Val	Ser	Glu	Ala		
				170					175					180		
Asp	Asp	Arg	Tyr	Ile	Cys	Asp	Arg	Phe	Tyr	Pro	Asn	Asp	Leu	Trp		
				185					190					195		
Val	Val	Val	Phe	Gln	Phe	Gln	His	Ile	Met	Val	Gly	Leu	Ile	Leu		
				200					205					210		

Pro Gly Ile Val	Ile Leu Ser Cys Tyr	Cys Ile Ile Ile Ser	Lys
215		220	225
Leu Ser His Ser	Lys Gly His Gln Lys	Arg Lys Ala Leu Lys	Thr
230		235	240
Thr Val Ile Leu	Ile Leu Ala Phe Phe	Ala Cys Trp Leu Pro	Tyr
245		250	255
Tyr Ile Gly Ile	Ser Ile Asp Ser Phe	Ile Leu Leu Glu Ile	Ile
260		265	270
Lys Gln Gly Cys	Glu Phe Glu Asn Thr	Val His Lys Trp Ile	Ser
275		280	285
Ile Thr Glu Ala	Leu Ala Phe Phe His	Cys Cys Leu Asn Pro	Ile
290		295	300
Leu Tyr Ala Phe	Leu Gly Ala Lys Phe	Lys Thr Ser Ala Gln	His
305		310	315
Ala Leu Thr Ser	Val Ser Arg Gly Ser	Ser Leu Lys Ile Leu	Ser
320		325	330
Lys Gly Lys Arg	Gly Gly His Ser Ser	Val Ser Thr Glu Ser	Glu
335		340	345
Ser Ser Ser Phe	His Ser Ser		
350			

<210> 2
 <211> 1588
 <212> DNA
 <213> Mus

<220>
 <221> CDS
 <222> (1)...(1059)

<400> 2
 atg gag ggg atc agt ata tac act tca gat aac tac acc gag gaa 45
 atg ggc tca ggg gac tat gac tcc atg aag gaa ccc tgt ttc cgt 90
 gaa gaa aat gct aat ttc aat aaa atc ttc ctg ccc acc atc tac 135
 tcc atc atc ttc tta act ggc att gtg ggc aat gga ttg gtc atc 180
 ctg gtc atg ggt tac cag aag aaa ctg aga agc atg acg gac aag 225
 tac agg ctg cac ctg tca gtg gcc gac ctc ctc ttt gtc atc acg 270
 ctt ccc ttc tgg gca gtt gat gcc gtg gca aac tgg tac ttt ggg 315
 aac ttc cta tgc aag gca gtc cat gtc atc tac aca gtc aac ctc 360
 tac agc agt gtc ctc atc ctg gcc ttc atc agt ctg gac cgc tac 405
 ctg gcc atc gtc cac gcc acc aac agt cag agg cca agg aag ctg 450
 ttg gct gaa aag gtg gtc tat gtt ggc gtc tgg atc cct gcc ctc 495
 ctg ctg act att ccc gac ttc atc ttt gcc aac gtc agt gag gca 540
 gat gac aga tat atc tgt gac cgc ttc tac ccc aat gac ttg tgg 585
 gtg gtt gtg ttc cag ttt cag cac atc atg gtt ggc ctt atc ctg 630
 cct ggt att gtc atc ctg tcc tgc tat tgc att atc atc tcc aag 675
 ctg tca cac tcc aag ggc cac cag aag cgc aag gcc ctc aag acc 720
 aca gtc atc ctc atc ctg gct ttc ttc gcc tgt tgg ctg cct tac 765
 tac att ggg atc agc atc gac tcc ttc atc ctc ctg gaa atc atc 810
 aag caa ggg tgt gag ttt gag aac act gtg cac aag tgg att tcc 855
 atc acc gag gcc cta gct ttc ttc cac tgt tgt ctg aac ccc atc 900
 ctc tat gct ttc ctt gga gcc aaa ttt aaa acc tct gcc cag cac 945
 gca ctc acc tct gtg agc aga ggg tcc agc ctc aag atc ctc tcc 990
 aaa gga aag cga ggt gga cat tca tct gtt tcc act gag tct gag 1035
 tct tca agt ttt gac tcc agc taa cacagatgta aaagactttt ttttat 1085
 acgataaata actttttttt aagttacaca tttttcagat ataaaagact gaccaatatt 1145

gtacagtttt tattgcttgt tggatttttg tcttgtgttt ctttagtttt tgtgaagttt 1205
aattgactta tttatataaa ttttttttgt ttcataattga tgtgtgtcta ggcaggacct 1265
gtggccaagt tcttagttgc tgtatgtctc gtggtaggac ttagaaaaag ggaactgaac 1325
attccagagc gtgtagttaa tcacgtaaaag ctagaaatga tccccagctg tttatgcata 1385
gataatctct ccattcccggt ggaacgtttt tctgttctt aagacgtgat tttgctgtag 1445
aagatggcac ttataaccaa agcccaaagt ggtatagaaa tgctgggttt tcaagttttca 1505
ggagtgggtt gatttcagca cctacagtgt acagtcttgt attaagttgt taataaaaagt 1565
acatgttaaa cttaaaaaaa aaa 1588

<210> 3
<211> 359
<212> PRT
<213> Mus

<400> 3
Met Glu Pro Ile Ser Val Ser Ile Tyr Thr Ser Asp Asn Tyr Ser
5 10 15
Glu Glu Val Gly Ser Gly Asp Tyr Asp Ser Asn Lys Glu Pro Cys
20 25 30
Phe Arg Asp Glu Asn Val His Phe Asn Arg Ile Phe Leu Pro Thr
35 40 45
Ile Tyr Phe Ile Ile Phe Leu Thr Gly Ile Val Gly Asn Gly Leu
50 55 60
Val Ile Leu Val Met Gly Tyr Gln Lys Lys Leu Arg Ser Met Thr
65 70 75
Asp Lys Tyr Arg Leu His Leu Ser Val Ala Asp Leu Leu Phe Val
80 85 90
Ile Thr Leu Pro Phe Trp Ala Val Asp Ala Met Ala Asp Trp Tyr
95 100 105
Phe Gly Lys Phe Leu Cys Lys Ala Val His Ile Ile Tyr Thr Val
110 115 120
Asn Leu Tyr Ser Ser Val Leu Ile Leu Ala Phe Ile Ser Leu Asp
125 130 135
Arg Tyr Leu Ala Ile Val His Ala Thr Asn Ser Gln Arg Pro Arg
140 145 150
Lys Leu Leu Ala Glu Lys Ala Val Tyr Val Gly Val Trp Ile Pro
155 160 165
Ala Leu Leu Leu Thr Ile Pro Asp Phe Ile Phe Ala Asp Val Ser
170 175 180
Gln Gly Asp Ile Ser Gln Gly Asp Asp Arg Tyr Ile Cys Asp Arg
185 190 195
Leu Tyr Pro Asp Ser Leu Trp Met Val Val Phe Gln Phe Gln His
200 205 210
Ile Met Val Gly Leu Ile Leu Pro Gly Ile Val Ile Leu Ser Cys
215 220 225
Tyr Cys Ile Ile Ile Ser Lys Leu Ser His Ser Lys Gly His Gln
230 235 240
Lys Arg Lys Ala Leu Lys Thr Thr Val Ile Leu Ile Leu Ala Phe
245 250 255
Phe Ala Cys Trp Leu Pro Tyr Tyr Val Gly Ile Ser Ile Asp Ser
260 265 270
Phe Ile Leu Leu Gly Val Ile Lys Gln Gly Cys Asp Phe Glu Ser
275 280 285
Ile Val His Lys Trp Ile Ser Ile Thr Glu Ala Leu Ala Phe Phe
290 295 300
His Cys Cys Leu Asn Pro Ile Leu Tyr Ala Phe Leu Gly Ala Lys

	305		310		315
Phe Lys Ser Ser	Ala Gln His Ala Leu	Asn Ser Met Ser Arg	Gly		
	320		325		330
Ser Ser Leu Lys	Ile Leu Ser Lys Gly	Lys Arg Gly Gly His	Ser		
	335		340		345
Ser Val Ser Thr	Glu Ser Glu Ser Ser	Ser Phe His Ser Ser			
	350		355		

<210> 4
 <211> 1758
 <212> DNA
 <213> Mus

<220>
 <221> CDS
 <222> (1)...(1080)
 <223>

<400> 4
 atg gaa ccg atc agt gtg agt ata tac act tct gat aac tac tct 45
 gaa gaa gtg ggg tct gga gac tat gac tcc aac aag gaa ccc tgc 90
 ttc cgg gat gaa aac gtc cat ttc aat agg atc ttc ctg ccc acc 135
 atc tac ttc atc atc ttc ttg act ggc ata gtc ggc aat gga ttg 180
 gtg atc ctg gtc atg ggt tac cag aag aag cta agg agc atg acg 225
 gac aag tac cgg ctg cac ctg tca gtg gct gac ctc ctc ttt gtc 270
 atc aca ctc ccc ttc tgg gca gtt gat gcc atg gct gac tgg tac 315
 ttt ggg aaa ttt ttg tgt aag gct gtc cat atc atc tac act gtc 360
 aac ctc tac agc agc gtt ctc atc ctg gcc ttc atc agc ctg gac 405
 cgg tac ctc gcc att gtc cac gcc acc aac agt caa agg cca agg 450
 aaa ctg ctg gct gaa aag gca gtc tat gtg ggc gtc tgg atc cca 495
 gcc ctc ctc ctg act ata cct gac ttc atc ttt gcc gac gtc agc 540
 cag ggg gac atc agt cag ggg gat gac agg tac atc tgt gac cgc 585
 ctt tac ccc gat agc ctg tgg atg gtg gtg ttt caa ttc cag cat 630
 ata atg gtg ggt ctc atc ctg ccc ggc atc gtc atc ctc tcc tgt 675
 tac tgc atc atc atc tct aag ctg tca cac tcc aag ggc cac cag 720
 aag cgc aag gcc ctc aag acg aca gtc atc ctc atc cta gct ttc 765
 ttt gcc tgc tgg ctg cca tat tat gtg ggg atc agc atc gac tcc 810
 ttc atc ctt ttg gga gtc atc aag caa gga tgt gac ttc gag agc 855
 att gtg cac aag tgg atc tcc atc aca gag gcc ctc gcc ttc ttc 900
 cac tgt tgc ctg aac ccc atc ctc tat gcc ttc ctc ggg gcc aag 945
 ttc aaa agc tct gcc cag cat gca ctc aac tcc atg agc aga ggc 990
 tcc agc ctc aag atc ctt tcc aaa gga aag cgg ggt gga cac tct 1035
 tcc gtc tcc acg gag tca gaa tcc tcc agt ttt cac tcc agc taa 1080
 cccttatgca aagacttata taatatatat atatatatga taaagaactt ttttatgtta 1140
 cacattttcc agatataaga gactgaccag tcttgtacag tttttttttt tttttaattg 1200
 actgttgga gtttatgttc ctctagtttt tgtgaggttt gacttaattt atataaatat 1260
 tgttttttgt ttgtttcatg tgaatgagcg tctaggcagg acctgtggcc aagttcttag 1320
 tagctgttta tctgtgtgta ggactgtaga actgtagagg aagaaactga acattccaga 1380
 atgtgtgga aattgaataa agctagccgt gatcctcagc tgttgctgca taatctcttc 1440
 attccgagga gcacccacc cccaccccca cccccacccc attcttaaat tgtttggtta 1500
 tgctgtgtga tggtttggtt ggtttttttt tgttggtgtt gttgtttttt ttttctgtaa 1560
 aagatggcac ttaaaaccaa agcctgaaat ggtggtagaa atgctggggt tttttttgtt 1620
 tgtttggttt ttcagttttt aagagtagat tgacttcagt ccctacaaat gtacagtctt 1680
 gtattacatt gttaataaaa gtcaatgata aacttaaaaa aaaaaaaaaa aaaaaaaaaa 1740
 aaaaaaaaaa aaaaaaaaaa 1758

<210> 5
 <211> 89
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Ligand peptide

<400> 5
 Met Asn Ala Lys Val Val Val Val Leu Val Leu Val Leu Thr Ala
 5 10 15
 Leu Cys Leu Ser Asp Gly Lys Pro Val Ser Leu Ser Tyr Arg Cys
 20 25 30
 Pro Cys Arg Phe Phe Glu Ser His Val Ala Arg Ala Asn Val Lys
 35 40 45
 His Leu Lys Ile Leu Asn Thr Pro Asn Cys Ala Leu Gln Ile Val
 50 55 60
 Ala Arg Leu Lys Asn Asn Asn Arg Gln Val Cys Ile Asp Pro Lys
 65 70 75
 Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn Lys
 80 85

<210> 6
 <211> 2244
 <212> DNA
 <213> Mus

<220>
 <221> CDS
 <222> (471)...(743)

<400> 6
 gcacgggaca ggccggggcca caccacccgg ggcgagctcg gagggcgggc ctctggggcg 60
 agggcccggc ggctcggccc agggcgcggtt acctcgtcgc cggggccgga gagggcgggc 120
 ggaggcacgg ggccctggagg cgccaggcgg aggatgcggg cgacacgggtg gcggcgggcga 180
 ccgcgcgacc gggcggggcgg gcgggcaggg gcgagcggag ggagggagcg gactgcggca 240
 ggatctgtcg aggaataatc ttgcggccgg cgattccccg cttttaagc gcagcctgca 300
 ctccccccac cccacgcagg ggcgggcctt ccccaacgcg ggcgcccact ggccgcgcgc 360
 cgccgctccc ctccagctcg cctgcgcctc tcactctccg tcagccgcat tgcccgtctg 420
 gcgtccggcc cccgaccgcg gctcgtccgc cgcccgcgc gcc 473
 atg aac gcc aag gtc gtg gtc gtg ctg gtc ctc gtg ctg acc gcg 518
 ctc tgc ctc agc gac ggg aag ccc gtc agc ctg agc tac aga tgc 563
 cca tgc cga ttc ttc gaa agc cat gtt gcc aga gcc aac gtc aag 608
 cat ctc aaa att ctc aac act cca aac tgt gcc ctt cag att gta 653
 gcc cgg ctg aag aac aac aac aga caa gtg tgc att gac ccg aag 698
 cta aag tgg att cag gag tac ctg gag aaa gct tta aac aag taa 743
 gcacaacagc caaaaaggac tttccgctag acccactcga ggaaaactaa aaccttgtga 803
 gagatgaaag ggcaaagacg tgggggaggg ggccttaacc atgaggacca ggtgtgtgtg 863
 tggggtgggc acattgatct gggatcgggc ctgaggtttg ccagcattta gaccctgcat 923
 ttatagcata cggtatgata ttgcagctta tattcatcca tgccctgtac ctgtgcacgt 983
 tggaattttt attactgggg tttttctaag aaagaaattg tattatcaac agcattttca 1043
 agcagttagt tccttcatga tcatcacaat catcatcatt ctcatctca ttttttaaa 1103
 caacgagtac ttcaagatct gaatttggct tgtttggagc atctcctctg ctcccctggg 1163
 gagtctgggc acagtcaggc ggtggcttaa caggagctg gaaaaagtgt cctttcttca 1223
 gacactgagg ctcccgcagc agcgcccctc ccaagaggaa ggcctctgtg gcactcagat 1283

```

accgactggg gctgggagcc gccactgcct tcacctcctc tttcaacctc agtgattggc 1343
tctgtgggct ccatgtagaa gccactatta ctgggactgt gctcagagac ccctctccca 1403
gctattccta ctctctcccc gactccgaga gcatgcatta atcttgcttc tgcttctcat 1463
ttctgtagcc tgatcagcgc cgcaccagcc gggaagaggg tgattgctgg ggctcgtgcc 1523
ctgcatccct ctctctccag ggctgcccc acagctcggg ccctctgtga gatccgtctt 1583
tggcctcctc cagaatggag ctggccctct cctggggatg tgtaatggtc cccctgctta 1643
cccgcaaaag acaagtcttt acagaatcaa atgcaatttt aaatctgaga gctcgctttg 1703
agtgactggg ttttgtgatt gcctctgaag cctatgtatg ccatggaggc actaacaac 1763
tctgaggttt ccgaaatcag aagcgaaaaa atcagtgaat aaaccatcat cttgccacta 1823
ccccctcctg aagccacagc agggtttcag gttccaatca gaactggttg caaggtgaca 1883
tttccatgca taaatgcat ccacagaagg tcctggtggt atttgtaact ttttgcaagg 1943
cattttttta tatatatttt tgtgcacatt tttttttacg tttctttaga aaacaaatgt 2003
atttcaaaat atatttatag tcgaacaatt catatatttg aagtggagcc atatgaatgt 2063
cagtagttta tacttctcta ttatctcaa ctactggcaa tttgtaaaga aatatatatg 2123
atatataaat gtgattgcag cttttcaatg ttagccacag tgtatttttt cacttgact 2183
aaaattgtat caaatgtgac attatatgca ctagcaataa aatgctaatt gtttcattgt 2243
a

```

<210> 7
 <211> 89
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Ligand peptide

```

<400> 7
Met Asp Ala Lys Val Val Ala Val Leu Ala Leu Val Leu Ala Ala
      5              10              15
Leu Cys Ile Ser Asp Gly Lys Pro Val Ser Leu Ser Tyr Arg Cys
      20              25              30
Pro Cys Arg Phe Phe Glu Ser His Ile Ala Arg Ala Asn Val Lys
      35              40              45
His Leu Lys Ile Leu Asn Thr Pro Asn Cys Ala Leu Gln Ile Val
      50              55              60
Ala Arg Leu Lys Asn Asn Arg Gln Val Cys Ile Asp Pro Lys
      65              70              75
Leu Lys Trp Ile Gln Glu Tyr Leu Glu Lys Ala Leu Asn Lys
      80              85

```

<210> 8
 <211> 1781
 <212> DNA
 <213> Mus

<220>
 <221> CDS
 <222> (82)...(351)

```

<400> 8
gaccatttcc cctctcgggc cacctcgggtg tcctcttgct gtccagctct gcagcctccg 60
gcgcgccttc ccgcccacgc c
      81
atg gac gcc aag gtc gtc gcc gtg ctg gcc ctg gtg ctg gcc gcg 126
ctc tgc atc agt gac ggt aaa cca gtc agc ctg agc tac cga tgc 171
ccc tgc cgg ttc ttc gag agc cac atc gcc aga gcc aac gtc aag 216

```

```

cat ctg aaa atc ctc aac act cca aac tgt gcc ctt cag att gtt 261
gca cgg ctg aag aac aac aac aga caa gtg tgc att gac ccg aaa 306
tta aag tgg atc caa gag tac ctg gag aaa gct tta aac aag taa 351
gcacaacagc ccaaaggact ttccagtaga cccccgagga aggctgacat ccgtgggaga 411
tgcaagggca gtggtgggga ggagggcctg aaccctggcc aggatggccg gcgggacagc 471
actgactggg gtcattgctaa ggtttgccag cataaagaca ctccgccata gcatatggta 531
cgatattgca gcttatattc atccctgccc tcgcccgtgc acaatggagc ttttataact 591
ggggtttttc taaggaattg tattacccta accagttagc ttcattccca ttctcctcat 651
cctcatcttc attttaaaaa gcagtgatta cttcaagggc tgtattcagt ttgctttgga 711
gcttctcttt gccctggggc ctctgggcac agttatagac ggtggctttg cagggagccc 771
tagagagaaa ccttccacca gagcagagtc cgaggaacgc tgcagggctt gtccctgcagg 831
gggcgctcct cgacagatgc cttgtcctga gtcaacacaa gatccggcag agggaggctc 891
ctttatccag ttcagtgccca gggtcgggaa gcttccttta gaagtgatcc ctgaagctgt 951
gctcagagac cctttcctag ccgttcctgc tctctgcttg cctccaaacg catgcttcat 1011
ctgacttccg cttctcacct ctgtagcctg acggaccaat gctgcaatgg aagggaggag 1071
agtgatgtgg ggtgccccct cctctctctc cctttgcttt cctctcactt gggccctttg 1131
tgagattttt ctttggcctc ctgtagaatg gagccagacc atcctggata atgtgagaac 1191
atgcctagat ttaccacaaa aacacaagtc tgagaattaa tcataaacgg aagtttaaat 1251
gaggatttgg accttggtaa ttgtccctga gtcctatata tttcaacagt ggctctatgg 1311
gctctgatcg aatatcagtg atgaaaataa taataataat aataataacg aataagccag 1371
aatcttgcca tgaagccaca gtggggattc tgggttccaa tcagaaatgg agacaagata 1431
aaacttgcat acattcttat gatcacagac ggccctgggtg gtttttggtg actatttaca 1491
aggcattttt ttacatatat ttttgtgcac tttttatgtt tctttggaag acaaatgtat 1551
ttcagaatat atttgtagtc aattcatata tttgaagtgg agccatagta atgccagtag 1611
atatctctat gatcttgagc tactggcaac ttgtaaaagaa atatatatga catataaatg 1671
tattgtagct ttccggtgtc agccacggtg tatttttcca cttggaatga aattgtatca 1731
actgtgacat tatatgcact agcaataaaa tgctaattgt ttcattgctgt 1781

```

```

<210> 9
<211> 4
<212> PRT
<213> Artificial Sequence

```

```

<220>
<223> added peptide

```

```

<400> 9
Arg Phe Lys Met

```

```

<210>10
<211> 4
<212> PRT
<213> Artificial Sequence

```

```

<220>
<223> added peptide

```

```

<400> 10
Arg Leu Lys Met

```

```

<210> 11
<211> 27
<212> DNA
<213> Artificial Sequence

```

<220>

<223> primer

<400> 11

tagcggccgc gttgcatgg aaccgat 27

<210> 12

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> primer

<400> 12

gcgtcgactt tgcataaggg ttagctg 27